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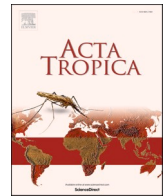
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# The HIV care continuum of Guinea-Bissau; Progress towards the UNAIDS 90-90-90 targets for HIV-1 and HIV-2

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## ABSTRACT

**Objective:** In the 2020 UNAIDS HIV treatment goals, 90% of people living with HIV (PLHIV) should be diagnosed, 90% of these should receive antiretroviral treatment (ART) and 90% of these should be virally suppressed. We aimed to evaluate whether Guinea-Bissau fulfills the 2020 treatment goals for both for HIV-1 and HIV-2.

**Design:** By combining data from a general population survey, treatment records from HIV clinics across Guinea-Bissau and a biobank from patients attending the largest HIV clinics in Bissau, we estimated each column of the 90-90-90 cascade.

**Method:** 2601 participated in the survey and were used to estimate the proportion of PLHIV who knew their HIV status and the proportion of PLHIV on ART. Answers given in the survey was verified with treatment records from HIV clinics. We measured viral load from biobank materials from HIV patients and estimated the proportion of virally suppressed PLHIV.

**Result:** 19.1% of PLHIV indicated to be aware of their HIV status. Of these, 48.5% received ART, and 76.4% of these were virally suppressed. For HIV-1 and HIV-1/2 the results were 21.2%, 40.9% and 75.1%. For HIV-2 the results were 15.9%, 63.6% and 80.7%. 26.9% of all HIV-1 infected in the survey were virologically suppressed, indicating that a much higher number of HIV-1 infected were aware of their status and on treatment.

**Conclusion:** Guinea-Bissau lags severely behind both the global and regional progress. Improvement in both testing and treating HIV is necessary to improve the quality of care.

## 1. Background

To effectively fight the HIV epidemic, UNAIDS set forth a series of treatment goals. By 2020, 90% of people living with HIV (PLHIV) should be diagnosed. Of these, 90% should be enrolled in Anti-Retroviral Treatment (ART) and 90% of these should be virally suppressed (UNAIDS, 2017). In total numbers, this corresponds to 90% of all PLHIV

knowing their HIV status, 81% of all PLHIV being on ART and 73% of all PLHIV being virally suppressed. The original goals set have since been updated and the global goals for 2025 is now 95–95–95 (UNAIDS, 2020). Globally, a recent UNAIDS report showed that 81% of PLHIV knew their HIV status, 67% of PLHIV were on ART and 59% of PLHIV were virally suppressed (WHO, 2020). The regional progress of West and Central Africa was reported by Marsh et al. to be 64%– 51% – 39%

**Abbreviations:** ART, anti retroviral treatment; FSW, female sex workers; HIV, human immunodeficiency virus; PLHIV, people living with HIV; WHO, World Health Organization.

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(Marsh et al., 2019). However, there are major information gaps with missing data from several countries.

Only a few countries, such as Sweden and Denmark, have the tools to make exact evaluations of their entire treatment system, due to their extensive and nationwide electronic medical record systems (Levi et al., 2016; Gisslén et al., 2017). In countries where the health system does not support such estimations, the WHO recommends pooling smaller cross-sectional studies to make estimation of each branch of the treatment cascade (Granich et al., 2017). Guinea-Bissau in West Africa has previously lacked the data and methods to make accurate HIV care estimations. Besides an examination of female sex workers (FSW) (Lindman et al., 2020), there has been no evaluation of the full treatment cascade.

The country struggles with poverty and political instability, conveying major health challenges for the health system (Galjour et al., 2021). Guinea-Bissau differs from other Sub-Saharan countries by having one of the world's highest prevalence's of HIV-2. HIV-2 is often overlooked but there is compelling evidence for making separate HIV-2 specific treatment evaluations (Ceccarelli et al., 2021; Gottlieb et al., 2018). A recent study from Senegal showed that around 76% of HIV-2 infected on ART were virally suppressed, but the study did not support a full treatment cascade evaluation (Raugi et al., 2020). To our knowledge, no accurate estimates of the full 90-90-90 treatment cascade for HIV-2 in the general population has previously been published.

The objective of this study was to evaluate the HIV detection, treatment and suppression rates (ie. the treatment cascade set forth by UNAIDS) in Bissau, the capitol of Guinea-Bissau and assess whether they live up to the 90-90-90 targets set forth by UNAIDS – both for HIV-1 and HIV-2.

## 2. Methods

To evaluate the treatment cascade, we used a combination of data sources from a prevalence survey and treatment information from the largest HIV clinic in Bissau.

### 2.1. Study populations

The prevalence survey;

In 2014–2016 a general population survey was performed in the suburbs of Bissau, an area under continuous demographic surveillance by the Bandim Health Project (BHP). Households were randomly selected using a random sample code in Stata (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP) to represent 10% of households, and all eligible inhabitants were invited to participate. In total 2601 participants were included, tested for HIV and had blood samples drawn. Blood samples were HIV typed and we measured viral load for PLHIV. All participants, regardless of HIV status, answered a questionnaire regarding demographic information, knowledge of HIV status, ART and co-morbidity. Further information regarding the survey can be found in the original article by Olesen et al. (2018).

The Bissau HIV cohort;

Since 2007, The Bandim Health Project (BHP) has continuously collected data from the largest HIV clinic Simão Mendes in the capitol Bissau. The cohort consists of an electronic database, where all patient files are continuously entered, and a biobank containing blood pellets from routine blood samples from patient attending the clinic (Jespersen et al., 2015). Blood samples were shipped for storage in Aarhus University Hospital, Denmark using dry-ice to maintain adequate cold-chain. In 2017, the electronic database was expanded to eight further clinics, giving information on current and past treatment via the medical records.

### 2.2. Data analyses

The initial column of the treatment cascade, the proportion of PLHIV who knew their HIV status, was calculated from the HIV survey as the number of participants who answered they knew they had HIV, divided by the total number of HIV positive individuals. Due to the high level of stigma and likely under-reporting of HIV from the survey, we sought to validate the self-reported survey answers with information from the database. As there are no unique identifiers for an individual in Guinea-Bissau, every HIV positive individual was manually searched for in the treatment record by using a combination of names, birthday, telephone number, ethnicity, and demographic information. If treatment records from patients participating in the survey were inconsistent with their answers in the survey, patients were reclassified to match the treatment record.

The second column of the treatment cascade, the proportion of PLHIV knowing their HIV status on ART, was calculated as the number of participants in the HIV survey self-reporting to be on ART treatment, divided by the number of HIV positive how knew their HIV status. These answers were also validated with treatment records from the HIV clinics.

The third column of the treatment cascade was estimated as the number of virally suppressed individuals among the participants receiving ART. All HIV positive from the survey had their viral load measured. The number of PLHIV to receive ART in the survey was low, and we therefore extended the estimates of viral suppression using biobank blood samples from PLHIV on ART from the HIV clinic at Hospital National Simão Mendes. To ensure the biobank blood samples were collected within the same timeframe as the estimates from the survey, we assessed the viral load from a random sample of patient blood samples collected in 2015 from patients with a minimum of 1-year treatment period, as recommended by WHO (2015). As viral load analyses are not routinely performed in Guinea-Bissau, blood samples were analyzed at Aalborg University Hospital, Denmark. Before viral load measurements all blood samples were HIV typed using the INNO-LIA HIV I/II Score (Fujirebio, Zwijndrecht, Belgium). RNA levels were measured using Abbot Real Time for HIV-1 whereas HIV-2 RNA was measured using an in-house method from Aalborg University Hospital previously described (Thomsen et al., 2018). A patient was considered virally suppressed if blood samples contained <1000 copies/ml as recommended by WHO (2016). All results were stratified by HIV type. However, as HIV-1 is more virulent and dominant subtype in double infected individuals, HIV-1 and HIV-1/2 double infected were joined into one group (Koblavi-Dème et al., 2004).

## 3. Results

This cross-sectional survey examining 2601 participants was performed from November 2014 to February 2016. The survey found that 4.0% of the population had HIV-1, and 2.8% had HIV-2 and 0.1% were dual-infected.

When validating answers given in the survey, 11 participants answered they did not know their HIV status, but when doing a manual search in the HIV databases, patient records were found stating they received previous tests and consultations in a HIV clinic and were therefore reclassified as knowing their HIV status. Two of these participants had active records at one of the HIV clinics stating they were receiving ART, and were therefore re-classified as receiving treatment.

The estimate for the first column showed that only 19.1% (33/173) of people identified with HIV in the survey knew their HIV status. Stratified by HIV status; among participants with HIV-1 or HIV-1/2 21.2% (22/104) were aware of their HIV infection, while 15.9% (11/69) of HIV-2 infected know their HIV status.

For the second column, 48.5% (16/33) of participants in the survey who knew their HIV status answered they were receiving ART. Among participants identified with HIV-1 and HIV-1/2, 40.9% (9/22) had initiated ART, while 63.6% (7/11) of participants with HIV-2 received

ART.

For the third column, 75.0% (12/16) of participants in the survey receiving ART were virally suppressed. For HIV-1 and HIV-1/2, 55.6% (5/9) were virally suppressed, while 7/7 (100%) of HIV-2 infected were suppressed. Of the total amount of PLHIV in the survey, 43.4% (75/173) were virally suppressed. Stratified by HIV type, 26.9% (28/104) of HIV-1 or HIV-1/2 infected were virally suppressed and 68.1% (47/69) of HIV-2 infected were virally suppressed.

We randomly selected 427 patients attending the HIV clinic at Simão Mendes, of whom 402 had sufficient blood samples available for viral load analysis. Of the 402, 69.9% (281/402) had HIV-1, 21.9% (88/402) had HIV-2 and 8.2% (33/402) were HIV-1/2 dual reactive. Overall, 76.4% (307/402) were virally suppressed. Divided by HIV type, 75.1% (236/314) of HIV-1 and HIV-1/2 infected and 80.7% (71/88) of HIV-2 infected were virally suppressed.

Using the results above, the overall progress towards 90–90–90 for Bissau, Guinea-Bissau in 2015: 19.1% were aware of their HIV status. 48.5% people knowing their HIV status were receiving ART and 76.4% of people receiving ART were virally suppressed. Of the total number of estimated PLHIV in Bissau, 19.1% indicated to know their HIV status, 9.2% indicated to receive ART and 43.3% are virally suppressed (Fig. 1). Stratified for HIV type, the results for HIV-1 & HIV-1/2 were 21.5%, 8.5% and 26.9% and 15.9%, 10.1% and 68.1% for HIV-2 (Fig. 2).

#### 4. Discussion

##### 4.1. Strengths and weaknesses

This study provides an estimate of the full treatment cascade for HIV in an urban Sub-Saharan African setting. This was possible due to a combination of a large HIV survey, years of continuous data collection from the largest HIV clinics in the country and a biobank containing blood samples. These sources did however have some limitations. For

the survey, several answers from participants were inconsistent with data from the medical records in a HIV clinic. We attempted to get more accurate estimates by manually searching for each HIV positive survey participant in the databases. As people in Guinea-Bissau do not have a unique identifier, but are sought for by combinations of name, birth date and other demographic factors, this may have missed some individuals, and thereby underestimated the 90-90-90 progress.

This study was based on the most recent HIV survey data available. Although the survey dates years back in time, we believe our results are still valid; our experience working at the nine largest HIV clinics tells us there have been no major improvements in test accessibility, medicine stock or patient compliance.

##### 4.2. Interpretation

Viral load results from the 402 patients from the largest HIV clinic in Bissau suggest that the estimates from the general HIV survey are reliable. With a viral suppression percentage of 76.4%, the gap to 90% viral suppression seems within reach. However, only patients receiving ART for more than one year were included, following the WHO guidelines. As such, the results should be interpreted as 76.4% of PLHIV who have been tested, linked to care and received ART for more than one year is virally suppressed. However, the viral suppression rate for all PLHIV participating in the survey was 43.3%. This relative high number should be interpreted with care as a large proportion of the infected have HIV-2. As previously described, a much higher rate of HIV-2 patients are Elite Controllers and would be virally suppressed even without treatment. In our study, 68.1% of all PLHIV-2 are virally suppressed while only 10.1% report being on ART. This corresponds with the previous understanding where as much as 25–50% of HIV-2 infected without ART had immeasurably low viral load, while the same was only true for <1% for HIV-1 (Raugi et al., 2020; Thomsen et al., 2018; Gottlieb et al., 2018). The viral suppression rate of all HIV-1 and HIV-1/2 infected who participated in

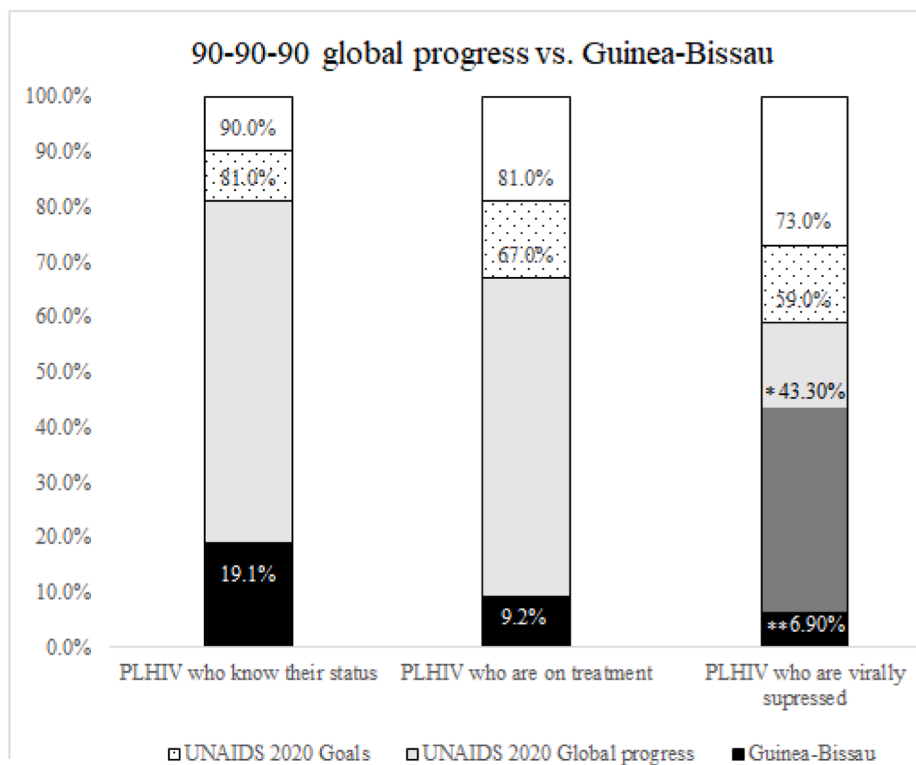
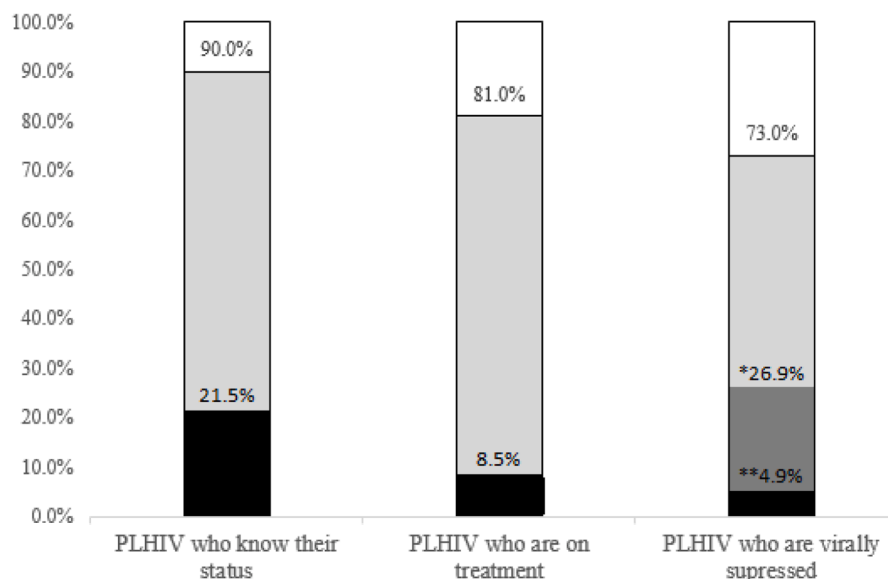


Fig. 1. 90-90-90 UNAIDS goals for diagnosis, treatment, and viral suppression. Goals compared to the global progress reported from the 2020 WHO progress report and the progress in Guinea-Bissau. As seen, Guinea-Bissau lags severely behind both the goals and the global progress in all three columns. \*Total percentage of PLHIV who are virally suppressed regardless of ART. \*\*Participants on ART who are virally suppressed.

(a) 90-90-90 HIV-1 & HIV-1/2 progress vs. goals



(b) 90-90-90 HIV-2 progress vs. goals

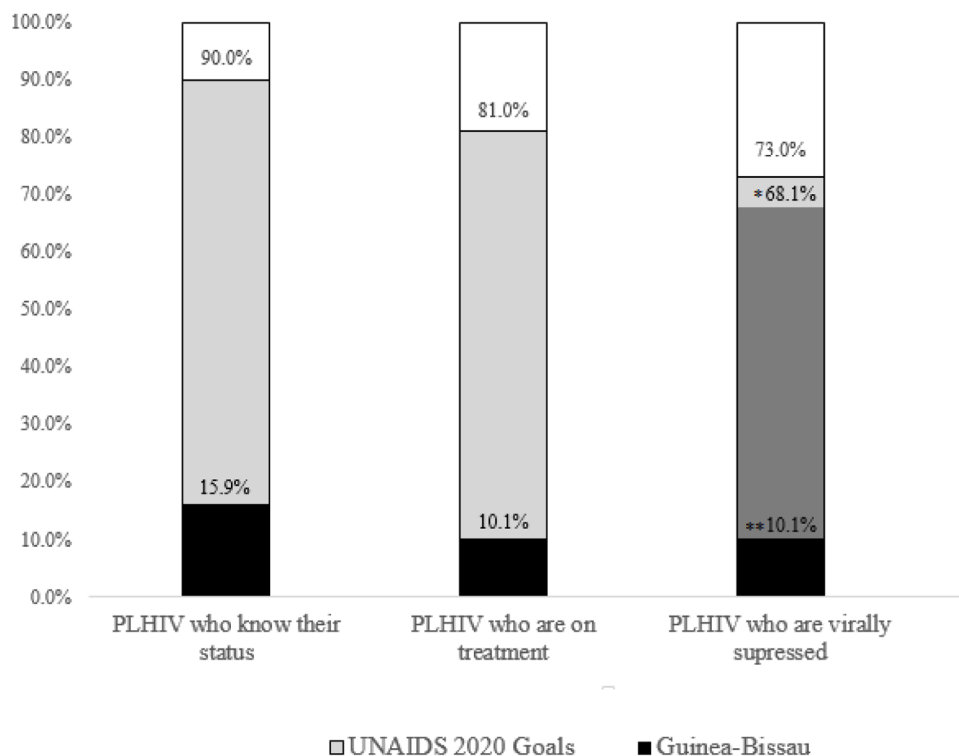


Fig. 2. 90-90-90 UNAIDS goals for diagnosis, treatment, and viral suppression compared to progress in Guinea-Bissau stratified by HIV type. \*Total percentage of PLHIV who are virally suppressed regardless of ART. \*\*Participants on ART who are virally suppressed.

the survey is also higher than the proportion of participants who report receiving treatment and this difference cannot be explained by Elite Controllers. Instead, it is more likely that participants in the survey underreported their HIV and their ART treatment status. The stigma associated with HIV is still high in Guinea-Bissau, and many patients fail even to inform their partners (Madsen et al., 2020). Nonetheless, we attempted to validate the HIV status by searching the database for treatment files for PLHIV screen-detected with HIV the survey. Although

the database covers the majority of PLHIV in the study area, it is possible to receive treatment from another clinic where we do not collect data, or even from abroad. The viral suppression rate of 26.1% of PLHIV-1 would suggest that a larger proportion are on treatment and a larger proportion are aware of their HIV status. If we apply the UNAIDS goals and assume that 90% of PLHIV on ART are virally suppressed then our suppression rate would correspond to 29.8% of PLHIV being on ART. In addition, if we assume that 90% of PLHIV who know their status receive ART this

would mean that 33.1% of PLHIV know their status. These numbers are only estimates, but does suggest that some participants answered incorrectly in the survey. As explained, the stigma towards HIV could explain this. While the progress towards 90–90–90 is better if we look at these estimates, it still describes a treatment cascade with challenges in all areas. These calculation were only performed for HIV-1 as we do not know how many PLHIV-2 are Elite Controllers.

It should also be noted that our results are from the capital Bissau where inhabitants have better access to healthcare compared to rural areas, which would likely show even lower suppression rates. The results of this poor quality of care becomes especially visible when looking at life expectancy of a 20 year old HIV infected in Guinea-Bissau, which is 9.8 years or only one fourth the life expectancy of the background population (Engell-Sørensen et al., 2021).

The only other examination of the HIV care continuum in Guinea-Bissau examined a group of FSW in Bissau (Lindman et al., 2020). Here, they found a higher rate of PLHIV who knew their HIV status and a higher use of ART. However, the viral suppression rates are similar to the rates we report for HIV-1 and HIV-1/2 double infected. A high-risk group, such as FSW would likely be tested more frequent compared to the background population, allowing them to seek treatment and therefore it is problematic to make direct comparisons to the background population.

To our knowledge, this is the first treatment evaluation for HIV-2 in the general population from any country. While the numbers of HIV-2 patients in the survey, are too low to make direct comparisons to HIV-1, it appears that HIV-2 infected patient on ART are more likely to be virally suppressed compared to the HIV-1 infected. This is supported by results from the biobank showing a slight difference where 75.1% of HIV-1 and HIV-1/2 infected and 80.7% of HIV-2 patients were virally suppressed. However, the numbers of individuals in the two groups are still small, and a more certain comparison would require larger numbers.

According to an UNAIDS report from 2020, the current worldwide progress is that around 81% of PLHIV know their HIV status. 67% of all PLHIV are on ART and 59% are virally suppressed (WHO, 2020). In West and Central Africa, around 68% of PLHIV know their HIV status. 58% are on ART and 45% are virally suppressed (WHO, 2020). While it is difficult to compare countries, even within the same region, our numbers for HIV-1 and HIV-1/2 infected suggest that Guinea-Bissau is well below the average progress in West Africa, and certainly lags behind in the global progress (Figs. 1 and 2). When comparing the continuums of other countries it is important to remember that this is the first study to include HIV-2, and only results for HIV-1 and HIV-1/2 are comparable.

## 5. Conclusions

Guinea-Bissau lags severely behind both regional and global progress in HIV care. If the 2025 goal of 95–95–95 should be fulfilled for Guinea-Bissau, this study suggests all areas of the treatment cascade need improvements. Efforts to test at-risk people should be intensified. People who are diagnosed with HIV should immediately receive ART and there is a critical need to increase treatment retention to reduce the number of patients who are lost-to-follow up (Hønge et al., 2013)

## Ethical approval statement

The study followed the standards provided by “The ethics of research related to healthcare in developing countries” by the Nuffield council on bioethics (McMillan and Conlon, 2004). Ethical approval has been given from the local ethics committee in the Ministry of Health in Guinea-Bissau (Ref<sup>o</sup> 070/CNES/INASA/2017).

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## Data sharing

Data from the current study cannot be made available online due to ethical and legal issues. However, researchers can request deidentified and summarized data from the corresponding author.

## CRediT authorship contribution statement

**Mads Mose Jensen:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft. **Stine Byberg:** Methodology, Formal analysis, Writing – review & editing. **Sanne Jespersen:** Methodology, Writing – review & editing. **Jens Steen Olesen:** Investigation, Writing – review & editing. **Zacarias José da Silva:** Investigation, Writing – review & editing. **Candida Medina:** Investigation, Writing – review & editing. **Henrik Krarup:** Resources, Writing – review & editing. **Christian Wejse:** Conceptualization, Methodology, Writing – review & editing. **Christian Erikstrup:** Conceptualization, Methodology, Writing – review & editing. **Bo Langhoff Hønge:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Writing – review & editing.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Data availability

The data that has been used is confidential.

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